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A Facile Aziridination of Allylic and Homoallylic Cyclic Acetals

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Abstract: Easy and fast aziridination of allylic and homoallylic acetals **2a**, **2b** and **2c** has been achieved by NsONHCO$_2$Et in the presence of solid K$_2$CO$_3$.

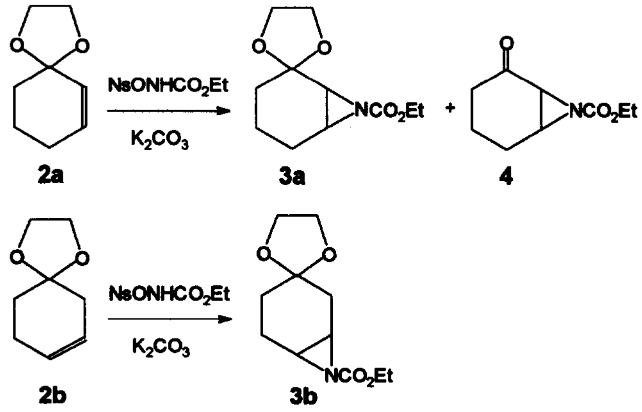
Nitrenes have been used in functionalisation reactions of nucleophilic sites, especially alkenes, to obtain aziridines, key intermediates in many reactions.[1]

Electron deficient alkenes, *i.e.* α,β-unsaturated esters or ketones, can be aziridinated in good yields by oxidative addition of various *N*-aminoheterocycles[2] and several nitrenes have been reported to add easily to different kind of alkenes.[3]

(Ethoxycarbonyl)nitrene (NCO$_2$Et) is known to add to α,β-unsaturated esters,[4] but in our experience[5] only with electron-rich alkenes, especially enamines, enols, silyl enol ethers, and silyl ketene acetals, it shows a good reactivity, while with allylic ethers[6] reacts sluggishly. Moreover our investigations of the regioselectivity in derivatives of geraniol or nerol have demonstrated the preferential addition of the nitrene to the double bond far from the oxygen atom.[7] The lower reactivity toward NCO$_2$Et of an allylic acetal with respect to cyclohexene has been also reported.[8]

In view of our interest in asymmetric synthesis,[5] we attempted to obtain the aziridination of chiral allylic acetals[9] and we planned to examine the best reaction conditions to get the functionalisation of the allylic double bond by the NCO$_2$Et.

We synthesised **2a** and **2b**, starting from 2-cyclohexenone;[10] then we tried to obtain **3a** and **3b**, by using ethyl *N*-{[(4-nitrophenyl)sulphonyl]oxy}carbamate (NsONHCO$_2$Et, **1**) at room temperature, first under homogeneous conditions, using Et$_3$N,[11] and then under phase-transfer catalysis conditions, using a 1M NaHCO$_3$ solution, in the presence of BnEt$_3$NCl.[12] Unfortunately in both cases the two substrates react sluggishly with NCO$_2$Et. We were not able to improve the yields of **3a** and **3b** (*ca* 5% GC) either increasing the molar ratio substrate : **1** : base up to 1 : 7 : 7 or reaction time to 96 h.[13]

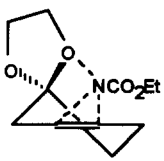


On the basis of our recent experiments,[14] we decided to use solid K$_2$CO$_3$ to deprotonate **1**.

The reaction with **2a** in CH$_2$Cl$_2$ at room temperature (molar ratio **2a** : **1** : K$_2$CO$_3$ = 1 : 6 : 6) gave, after 3.5 h, the expected aziridine **3a**[15] in 30% yield. Another product **4** (10% yield) could be isolated by flash-chromatography on silica gel (hexane : ethyl acetate = 7 : 3); it may come from hydrolysis of **3a**.[16]

The reaction with **2b**, in the same conditions, gave exclusively the aziridine **3b** (62% yield) in only 1 h.

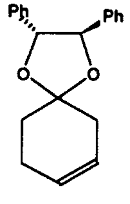
In this way the use of a solid base, without catalyst,[17] gave, with good yields and in short reaction times, an efficient aziridination of the double bond, which do not react easily with NCO_2Et, generated by $NsONHCO_2Et$ in the usual conditions.



To explain the different reactivity between **2a** and **2b** we believe that, in addition to electronic reasons,[18] a coordination of NCO_2Et by the acetal oxygen atoms might be preferred in the substrate **2b**,[19] as shown on the left.

Mash in methylene transfer to chiral allylic acetals[20] proposed that dioxolane oxygen atoms play a basic role in the observed stereochemical course of the reactions, presumably due to analogous reasons.

Stimulated by these results, we synthesised the chiral homoallylic acetal **2c** in order to achieve a diastereoselective aziridination, according to reaction conditions reported in this work. The first data (d.e. 51%) are encouraging and are still object of our investigations.



2c

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